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OMB No. 0704-0188 Public reporting burden for this collection of information is estimated to average 1 hour per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden, to Washington Headquarters Services, Directorate for Information Operations and Reports, 1215 Jefferson Davis Highway, Suite 1204, Arlington, VA 22202-4302, and to the Office of Management and Budget, Paperwork Reduction Project (0704-0188), Washington, DC 20503. 1. AGENCY USE ONLY (Leave blank) 2. REPORT DATE 3. REPORT TYPE AND DATES COVERED April 2006 **USARIEM Technical Report** 4. TITLE AND SUBTITLE 5. FUNDING NUMBERS Seven Days of Intermittent Altitude Exposures Improve Endurance Performanct at 6. AUTHOR(S) B.A. Beidleman; S.R. Muza; C.S. Fulco; A. Cymerman; M.N. Sawka; S.F. Lewis, G.S. Skrinar 7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES) 8. PERFORMING ORGANIZATION Thermal & Mountain Medicine Division REPORT NUMBER U.S. Army Research Institute of Environmental Medicine T06-05 Kansas Street Natick, MA 01760-5007 9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES) 10. SPONSORING / MONITORING Same as #7 above AGENCY REPORT NUMBER 11. SUPPLEMENTARY NOTES 12a. DISTRIBUTION / AVAILABILITY STATEMENT 12b. DISTRIBUTION CODE Distribution is unlimited. 13. ABSTRACT (Maximum 200 words) The purpose of this study was to determine if seven days of intermittent altitude exposures (IAE), in combination with either res or exercise training, could improve endurance performance and induce physiologic adaptations that are consistent with altitude acclimatization at 4300 m. Ten adult lowlanders (26±2 yrs; 77±4 kg; 174±3 cm; means ±SE) completed a cycle endurance test. The cycle endurance test consisted of two continuous steady-state exercise bouts (15 min at 40% and 70% altitude-specific peak oxygen uptake (V?O2peak)) followed immediately by a time-trial performance test (time to complete a standardized amount of work on a cycle ergometer) during an acute exposure to 4300 m altitude-equivalent (446 mmHg) once before (PreIAE) and once after (PostIAE) 7 d of IAE (4 hod-1, 5 dowk-1, 4300 m). During each IAE, five subjects performed exercise training (45-60 minod-1 at 60%-70% of V?O2peak) and five subjects rested. Both groups demonstrated similar improvements in time trial performance and physiologic adaptations during rest and steady-state exercise from PreIAE to PostIAE. Thus, data from all subjects were combined. Seven days of IAE resulted in 1) a 16% improvement (P<0.05) in time-trial performance from PreIAE (35.3±2.6 min) to PostIAE (29.2±1.9 min), 2) a 4% improvement (P<0.05) in exercise arterial O2 saturation from PreIAE (77±2 %) to PostIAE (80±2 %), 3) a 15% reduction (P<0.05) in exercise heart rate from PreIAE (136±6 bpm) to PostIAE (116±6 bpm), and 4) a 22% reduction (P<0.05) in exercise rating of perceived exertion from PreIAE (10 ± 1) to PostIAE (8 ± 1). Our findings suggest that 7 d of IAE, in combination with either rest or exercise training, will improve time-trial performance and induce physiologic adaptations during rest and steady-state exercise consistent with altitude acclimatization at 4300 m. 14. SUBJECT TERMS 15. NUMBER OF PAGES Hypobaric hypoxia, intermittent hypoxia, cycle time trial, arterial oxygen saturation 19 16. PRICE CODE 17. SECURITY CLASSIFICATION 18. SECURITY CLASSIFICATION 20. LIMITATION OF ABSTRACT 19. SECURITY CLASSIFICATION

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SEVEN DAYS OF INTERMITTENT ALTITUDE EXPOSURES IMPROVE ENDURANCE PERFORMANCE AT 4300 M

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BACKGROUND

Numerous regions of geopolitical interest, such as Central and West Asia, the Balkans, and South America, contain extensive areas of moderate (1500 m to 3500 m) to high (3500 m to 5500 m) altitudes. These mountain ranges form the borders of nations, provide sanctuary for hostile forces, and are likely settings for various types of military operations involving military personnel. Although the mountain environment presents a likely setting for military operations, U.S. military technological superiority is lessened in the mountain environment due to limited ability to utilize air support and crew-served combat vehicles. In the mountain environment, therefore, the burden of combat relies heavily on the fighting ability of the dismounted Warfighter.

Endurance performance, however, is degraded in the unacclimatized person rapidly deployed to high mountain environments due to the lower partial pressure of O_2 in the ambient air. Endurance performance improves following 2 to 3 wk of continuous altitude residence, as the body adapts to the lower partial pressure of O_2 . However, soldiers rapidly deployed to altitude may not have sufficient time to gain the benefits of altitude acclimatization induced by 2 to 3 wk of continuous altitude residence. Therefore, attempts to pre-acclimatize individuals before ascent to high altitude using daily intermittent exposure to either hypoxia or hypobaric hypoxia have gained interest.

Recent studies demonstrated that 15 d of intermittent altitude exposures (IAE) (4 h•d⁻¹, 5 d•wk⁻¹, 4300 m) was equally as effective as continuous altitude residence in improving endurance performance, and inducing physiologic adaptations consistent with altitude acclimatization at 4300 m. However, current military requirements emphasize short notification and rapid deployment. Thus, a 3-wk IAE approach of preacclimatization to altitude may be too long of a time period to meet current military requirements. The purpose of this study was to determine whether 7 d of IAE (4 h•d⁻¹, 5 d•wk⁻¹, 4300 m), in combination with either rest or exercise training, could also improve endurance performance and induce physiologic adaptations consistent with altitude acclimatization at 4300 m. Validating this approach to altitude acclimatization should lead to an effective but shorter IAE treatment regimen that will minimize the decrement in endurance performance during military missions in high mountainous regions, and also meet military requirements for short notification and rapid deployment.

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EXECUTIVE SUMMARY

Endurance performance is degraded in military personnel acutely deployed to high mountain environments. Although endurance performance improves following altitude acclimatization induced by 2 to 3 wk of continuous altitude residence, soldiers rapidly deployed to altitude may not have sufficient time to gain the benefits of altitude acclimatization. Recent studies demonstrated that 15 d of intermittent altitude exposures (IAE) was as effective as continuous altitude residence in improving endurance performance, and inducing physiologic adaptations consistent with altitude acclimatization at 4300 m. The purpose of this study was to determine if 7 d of IAE, in combination with either rest or exercise training, could improve endurance performance and induce physiologic adaptations that are consistent with altitude acclimatization at 4300 m. Ten adult lowlanders (26±2 yrs; 77±4 kg; 174±3 cm; means ±SE) completed a cycle endurance test. The cycle endurance test consisted of two continuous steadystate exercise bouts (15 min at 40% and 70% altitude-specific peak oxygen uptake (V O_{2peak})) followed immediately by a time-trial performance test (time to complete a standardized amount of work on a cycle ergometer) during an acute exposure to 4300 m altitude-equivalent (446 mmHg) once before (PreIAE) and once after (PostIAE) 7 d of IAE (4 h•d⁻¹, 5 d•wk⁻¹, 4300 m). During each IAE, five subjects performed exercise training (45-60 min•d⁻¹ at 60%-70% of VO_{2peak}) and five subjects rested. Both groups demonstrated similar improvements in time trial performance and physiologic adaptations during rest and steady-state exercise from PreIAE to PostIAE. Thus, data from all subjects were combined. Seven days of IAE resulted in 1) a 16% improvement (P<0.05) in time-trial performance from PreIAE (35.3±2.6 min) to PostIAE (29.2±1.9 min), 2) a 4% improvement (P<0.05) in exercise arterial O₂ saturation from PreIAE (77±2 %) to PostIAE (80±2 %), 3) a 15% reduction (P<0.05) in exercise heart rate from PreIAE (136±6 bpm) to PostIAE (116±6 bpm), and 4) a 22% reduction (P<0.05) in exercise rating of perceived exertion from PreIAE (10±1) to PostIAE (8±1). Our findings suggest that 7 d of IAE, in combination with either rest or exercise training, will improve time-trial performance and induce physiologic adaptations during rest and steady-state exercise consistent with altitude acclimatization at 4300 m.

INTRODUCTION

Unacclimatized lowlanders experience marked decrements in both maximal and submaximal exercise performances with rapid ascent to high altitude (9). The reduction in atmospheric pressure at high altitude reduces the arterial oxygen content and proportionally oxygen delivery to the muscle (20, 21). As a consequence, maximal oxygen uptake (VO_{2max}) declines with increasing altitude (1, 7, 22, 23). In contrast, oxygen uptake for any submaximal power output is independent of elevation (14, 17). Expressed in relative terms, a given submaximal oxygen uptake at altitude represents a greater percentage of the reduced VO_{2max}. The practical implication is that tasks that require a fixed amount of exercise or work to be performed as quickly as possible (e.g., traveling from point A to B or unpacking a military supply truck) will take a greater length of time at altitude compared to sea level. For example, relative to sea level, at 4300 m there is a 60% to 70% increase in the time to complete a 200 kJ to 720 kJ cycle time-trial performance test (3, 8). Similarly, there is a 40% increase in the best times to complete a marathon at 4300 m compared to sea level (15).

Although maximal exercise performance does not improve following continuous altitude residence (26), 20% to 60% improvements in submaximal endurance performance occur following altitude acclimatization induced by 2 to 3 wk of continuous altitude residence (8, 11, 13). Athletes, soldiers, and mountaineers rapidly deployed to altitude, however, may not have sufficient time or opportunity to complete traditional altitude acclimatization programs. Therefore, attempts to pre-acclimatize individuals before ascent to high altitude using daily intermittent exposure to either hypoxia or hypobaric hypoxia have gained interest (2, 3, 18, 19). A recent study demonstrated that 15 d of intermittent altitude exposures (IAE) (4 h•d⁻¹, 5 d•wk⁻¹, 4300 m) was as effective as continuous altitude residence in improving endurance performance, and inducing physiologic adaptations consistent with altitude acclimatization at 4300 m (3). However, current military requirements emphasize short notification and rapid deployment and 15 d of IAE may not meet this requirement.

The purpose of this study was to determine whether 7 d of IAE (4 h•d⁻¹, 5 d•wk⁻¹, 4300 m), in combination with either rest or exercise training, could improve endurance performance and induce physiologic adaptations consistent with altitude acclimatization at 4300 m. We hypothesized that 7 d of IAE would improve time-trial performance and physiologic adaptations during rest and steady-state exercise at 4300 m by approximately half of the improvements reported following 15 d of IAE (3). We also hypothesized that exercise training during IAE would improve time-trial performance more than rest alone due to a greater hypoxic stimulus resulting from exacerbation of arterial hypoxemia during exercise training.

METHODS

SUBJECTS

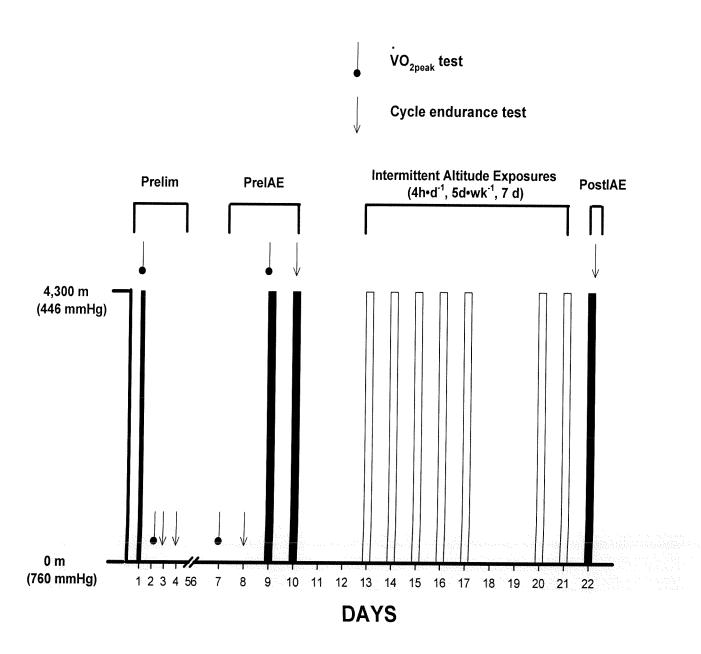
Ten nonsmoking volunteers (8 men, 2 women) with a mean (±SE) age, body weight, and height of 26±2 yr, 77±4 kg, 174±3 cm, respectively, completed this study. Each was a lifelong low-altitude resident and had no exposure to altitudes greater than 1,000 m for at least 6 mo immediately preceding the study. All volunteers received medical examinations, and none had any condition warranting exclusion from the study. All tested within normal ranges for pulmonary function. All had normal hemoglobin concentration and serum ferritin levels. The women had a normal menstrual cycle length (28±1 d) over the 2-mo testing period, had not taken oral contraceptives or hormone therapy for the previous 6 mo, and had never been pregnant. Testing was not controlled for menstrual cycle phase because of the reported lack of menstrual cycle effect on physical performance at altitude (4). All volunteers participated in regular sea level aerobic training (1-2 h•wk⁻¹) during the 2-mo study. Each gave written and verbal acknowledgment of their informed consent and was made aware of their right to withdraw without prejudice at any time. Investigators adhered to the policies for protection of human subjects as prescribed in Army Regulation 70-25, and the research was conducted in adherence with the provisions of 45 CFR Part 46.

PROTOCOL

Design

This study utilized an unblinded two factor (test condition and group) experimental design. The test conditions were defined as sea level (SL), before IAE (PreIAE), and after IAE (PostIAE). The groups were defined as rest and exercise training during IAE. Each volunteer completed a cycle endurance test. The cycle endurance test consisted of two continuous steady-state exercise bouts (15 min at 40% and 70% altitude-specific VO_{2max}) followed immediately by a time trial performance test (time to complete a standardized amount of work on a cycle ergometer) during an acute exposure to 4300 m altitude-equivalent (446 mmHg) once before (PreIAE) and once after (PostIAE) 7 d of IAE (4 h•d⁻¹, 5 d•wk⁻¹, 4300 m) (Figure 1). To minimize the impact of potential learning effects, all volunteers performed two preliminary VO_{2max} (one at 4,300 m and one at SL) and two cycle endurance tests (both at SL) before definitive data collection.

Figure 1. Study design



Each test volunteer's peak oxygen uptake (VO_{2peak}) and cycle endurance were evaluated in the preliminary phase (Prelim), at sea level (SL), before intermittent altitude exposures (PrelAE), and after intermittent altitude exposures (PostIAE).

Intermittent Altitude Exposures

Volunteers were weighed in the morning before each IAE (wearing t-shirts, shorts, and socks) and were encouraged to maintain constant body weight throughout the study. During each 4-h IAE, five volunteers rested for the entire 4-h altitude exposure. In contrast, the other five volunteers exercised on a cycle ergometer for ~45-60 min at 70% to 85% of pre-training altitude maximal heart rate and then rested for the remainder of the 4-h altitude exposure. As exercise training progressed, power output was increased, if necessary, to ensure achievement of appropriate training heart rate (HR) during each training session. Arterial oxygen saturation (SaO₂) using a finger pulse oximeter (Model N-200, Nellcor, Pleasanton, CA), and HR using a wireless heart rate watch (Model 8799, Computer Instruments Co, Hempstead, NY) were periodically measured on both groups of volunteers.

At the end of each altitude exposure, all volunteers remained resting in the hypobaric chamber so that their total exposure time to hypobaric hypoxia, including a 15-min decompression and 15-min recompression was 4 h•d⁻¹. Volunteers were weighed at the end of each 4-h altitude exposure and encouraged to drink water to replace any fluid loss during exercise and/or altitude exposure. All volunteers were required to maintain (i.e., not increase or decrease) their 1-2 h•wk⁻¹ of personal exercise training at SL to maintain their pre-study level of physical fitness. Physical activity monitor logs were kept throughout the 5-wk study.

Environmental Conditions

All testing and training were performed in a hypobaric chamber maintained at a temperature and relative humidity of 21±2°C and 45±5%, respectively. The SL testing was performed at ambient barometric pressure (~760 mm Hg), and all altitude exposures were conducted at an altitude-equivalent of 4300 m (~446 mmHg).

Exercise Testing

Prior to each exercise test on an electromagnetically-braked cycle ergometer (Model 800s, Sensormedics Co, Yorba Linda, CA), the volunteer was weighed (wearing t-shirt, shorts, and socks) to the nearest 0.1 kg. For each exercise test, HR was

determined from continuous ECG recordings (Cardiovit AT-6C; Schiller Canada, Inc., Nepean, Ontario), SaO₂ was measured by finger pulse oximetry (Model N-200, Nellcor, Pleasanton, CA), ratings of perceived exertion (RPE) were measured using the 6 to 20 Borg Scale (5) and systolic blood pressure (SBP) and diastolic blood pressure (DBP) were measured using an automated system (Model 4240, Suntech, Raleigh, NC). Respiratory gas measurements (i.e., VE, VO₂, VCO₂) were made in the mixing-chamber mode using an open-circuit metabolic measurement system (Vmax 229, Sensormedics Co, Yorba Linda, CA) calibrated with certified gases and volume standard. The respiratory exchange ratio (RER) was calculated from VO₂ and VCO₂ measurements. The ventilatory equivalent for CO₂ (VE•VCO₂-1) was calculated from each subject's VE and VCO₂ data. Mean arterial pressure (MAP) was calculated as 0.333 (SBP-DBP)+DBP.

Volunteers were given meals of identical nutrient and caloric content before each exercise test. Volunteers consumed 5 ml water•kg body weight⁻¹ one hour before beginning the cycle endurance test and were allowed to drink ad libitum during the cycle endurance test. Volunteers were required to abstain from caffeine, alcohol, and tobacco for at least 24 h prior to each exercise test and not exercise on the testing day. Each exercise test was conducted approximately the same time of day and same number of hours after eating.

Peak Oxygen Uptake (VO_{2peak}) Test. VO_{2peak} was measured during incremental, progressive cycling exercise to exhaustion. The VO_{2peak} test consisted of 3 min of rest, a 3-min warm-up at 60 W, 2 min at 80-100 W for women or 120-150 W for men, and an increase in work rate every 2 min by 25-30 W until volunteers were unable to maintain a constant pedaling rate of 60 rpm.

Cycle Endurance Test. The cycle endurance test consisted of 5 min of rest, a 5-min warm-up at 50 W, and two consecutive steady-state exercise bouts (15 min at 40% and 70% altitude-specific VO_{2max}) followed immediately by a time-trial performance test (time to complete a fixed amount of work on a cycle ergometer). The time to complete a fixed amount of work on a cycle ergometer, consisting of 216 kJ of total work for men and 156 kJ of total work for women, was used as a measure of time-trial performance. A shorter time from one testing condition to the next was considered an improvement in performance and vice-versa. During the time-trial performance test,

volunteers were free to manually increase or decrease the work rate on the cycle ergometer by 5 W increments. There were no restrictions on the number of 5 W changes or their direction. This type of time-trial performance test has been shown to have a high repeatability and low coefficient of variation (12). Respiratory gas measurements were made at rest and during the two steady-state exercise bouts but not during the time-trial portion of the cycle endurance test.

STATISTICS

A two-way repeated-measures ANOVA was used to analyze differences between the independent group factor (rest and exercise training) and repeated measures test condition factor (SL, PreIAE, and PostIAE) for all measurements. Three-way ANOVAs, with repeated measures on the additional factor of exercise duration, were used for physiological measurements made during the cycle endurance test. Significant main effects and interactions were analyzed using Tukey's least significant difference test. Pearson-product moment correlation coefficients were calculated for the relationships between changes in time-trial performance and changes in 1) resting and exercise SaO₂, 2) resting and exercise RER, 3) resting and exercise HR, 4) resting and exercise MAP, and 5) resting and exercise RPE. Statistical significance was set at P < 0.05. All data are presented as means \pm SE.

RESULTS

Although arterial O₂ desaturation was 5%-10% greater in the exercise training compared to the resting group during the exercise-training portion of each IAE, both groups demonstrated similar improvements in time-trial performance and physiologic adaptations at rest and during steady-state exercise from PreIAE to PostIAE. Thus, for statistical analyses, data from all ten subjects were combined. For time-trial performance, individual responses are provided.

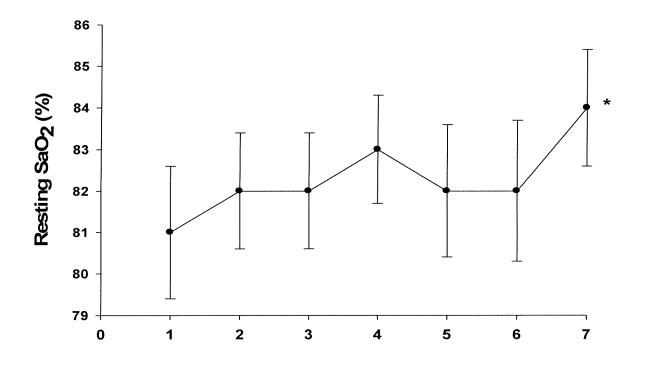
VOLUNTEER TEST SUBJECTS

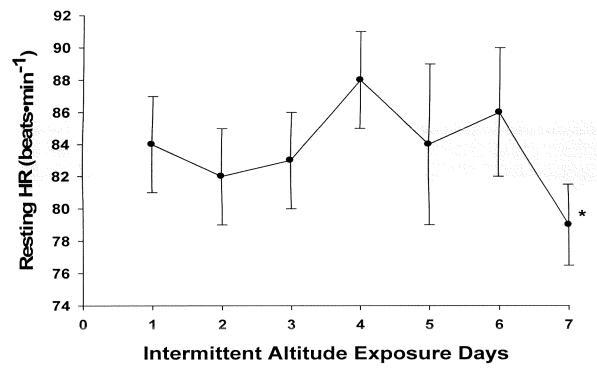
Mean body weights, heights, and energy intakes were not different between test conditions. Time spent performing personal exercise training at SL per week did not change from baseline during the 3-wk course of the study.

INTERMITTENT ALTITUDE EXPOSURES

Figure 2 provides the mean daily resting SaO2 and heart rate for the seven days of IHE. Resting SaO_2 increased (P<0.05) in a steady fashion while resting HR demonstrated considerable variability but decreased (P<0.05) from day 1 to day 7 of IAE.

Figure 2. Daily resting arterial oxygen saturation (SaO₂) and heart rate (HR)





PEAK OXYGEN UPTAKE TEST

The VO_{2peak} (ml•kg⁻¹•min⁻¹) decreased 22% (P<0.05) from SL (43.9±2.2) to PreIAE (34.2±2.0). The VO_{2peak} was not measured at PostIAE.

CYCLE ENDURANCE TEST

Steady-State Exercise

Ventilatory and cardiovascular responses, measured at rest and 40% and 70% of altitude-specific VO_{2max} during the steady-state portion of the cycle endurance test are presented in Table 1. From SL to PreIAE, resting VO₂ remained the same but exercise VO₂ at 40% and 70% altitude-specific VO_{2max} decreased (P<0.05). Resting and exercise VO₂ remained unchanged from PreIAE to PostIAE. From SL to PreIAE, resting and exercise VE•VCO₂-¹ increased (P<0.05), but remained unchanged from PreIAE to PostIAE. From SL to PreIAE, resting and exercise SaO₂ decreased (P<0.05). Resting and exercise SaO₂ increased (P<0.05) 4% from PreIAE to PostIAE. From SL to PreIAE, resting and exercise RER decreased (P<0.05). Resting and exercise RER decreased (P<0.05) 6% from PreIAE to PostIAE.

From SL to PreIAE, resting and exercise HR at 40% altitude-specific VO $_{2max}$ increased (P<0.05). Resting HR decreased (P<0.05) 20% while exercise HR at 40% and 70% altitude-specific VO $_{2max}$ decreased (P<0.05) 15% and 5%, respectively from PreIAE to PostIAE. From SL to PreIAE, resting and exercise MAP at 40% altitude-specific VO $_{2max}$ did not change but exercise MAP at 70% altitude-specific VO $_{2max}$ decreased (P<0.05). Resting and exercise MAP at 40% altitude-specific VO $_{2max}$ decreased (P<0.05) 5% while exercise MAP at 70% altitude-specific VO $_{2max}$ did not change from PreIAE to PostIAE. From SL to PreIAE, resting RPE did not change but exercise RPE at 40% and 70% altitude-specific VO $_{2max}$ increased (P<0.05). Resting RPE did not change but exercise RPE at 40% and 70% altitude-specific VO $_{2max}$ decreased (P<0.05) 20% and 21%, respectively, from PreIAE to PostIAE.

Time-Trial Performance Test

Individual (top) and group (bottom) time-trial performance data are presented in Figure 3. All individuals exhibited a decrement in time-trial performance (i.e., increase in time) from SL to PreIAE. The group exhibited a $66\pm10\%$ decrement (P<0.05) in time-trial performance (min) from SL (21.4 ±1.3) to PreIAE (35.3 ±2.6). Nine of the ten subjects exhibited an improvement in time-trial performance (i.e., decrease in time) from PreIAE to PostIAE. The group exhibited a16% improvement (P<0.05) in time-trial performance from PreIAE to PostIAE (29.2 ±1.9). There was no correlation between individual improvement in time-trial performance from PreIAE to PostIAE with the improvement in 1) resting or exercise SaO₂, 2) resting or exercise RER, 3) resting or exercise HR, 4) resting or exercise MAP, or 5) resting or exercise RPE. The improvement in time-trial performance and improvement in exercise SaO₂ at 70% of altitude-specific VO_{2peak} from PreIAE to PostIAE demonstrated a trend towards significance (P=0.06).